REMARKS/ARGUMENTS

Status of the Claims

Claims 1-9 and 11-20 are currently pending. Claims 11-20 stand withdrawn. The objection set forth in the Office Action Mailed August 28, 2006 has been overcome by amendment as stated below. The rejections set forth in the Office Action Mailed August 28, 2006 are traversed by Applicants' arguments set forth below.

1. Claim Objections

Claim 1 is objected to because of a typographical error. The Patent Office states that claim 1, line 21 should read "sample is ***greater*** than the level of nuclear localization" rather than "sample is ***great*** than the level of nuclear localization." Applicants have amended Claim 1 accordingly, thereby obviating the objection.

2. Claim rejections under 35 USC §112 first paragraph

Claims 1-9 and 11-20 are rejected under 35 USC §112 first paragraph for failing to meet the enablement requirement. Applicants respectfully point out that claims 11-20 are currently withdrawn, and therefore the rejections relating to those claims are moot at this time. Thus, Applicants' discussion below does not address the rejections in the Office Action that specifically relate to claims 11-20.

The Action states that claim 1 is enabled "for a method for making a prognosis of disease course in human breast or prostate cancer patient comprising steps (a) through (d)", but is not enabled for preparing a prognostic index as recited in step (e). The Action then discusses the claims in view of several Wands factors.

The nature and breadth of the claims:

The Action states that the claims are broadly recited and are not commensurate in scope with the specification. However, the claims are particularly drawn to making a prognosis for human breast or prostate cancer patients. The specification provides

Examples of applying the method of the claims to both breast and prostate cancer patients. Thus, the claims are commensurate in scope with the specification.

The state of the prior art and the level of predictability in the prior art:

The Action discusses three references, including Hedge *et al.*, Oshika *et al.*, and Salveson *et al.* The Action asserts that the references teach "that the claimed prognostic index would not" be "predictive for all cancer types." However, as discussed above, claims 1-9 are drawn to breast and prostate cancers, not to "all cancer types." The Examples in the specification provide ample evidence that the prognostic index ***is*** predictive for the cancer types of claims 1-9. The references cited in the Action do not demonstrate, teach, or suggest that the prognostic method of the claims cannot be used in prognosis of breast and prostate cancers.

The amount of direction provided by the inventor and the existence of working examples:

The Action asserts that "it is not clear exactly how the prognosis is intended to be made using the claimed index in claim 1." The Action goes on to state that the specification "would not have taught one skilled in the art how to make and/or use the full scope of the claimed inventions without undue experimentation." Applicants respectfully point out that the specification provides specific Examples of how to make and use the prognostic index of claim 1. In particular, Examples 1 and 2 detail the steps involved in the construction and use of a tumor prognostic index in breast cancer, and Example 3 provides similar specific details on the construction of a prognostic index in prostate cancer, as well as statistical evidence validating this index as a reliable predictor of disease progression. Furthermore, the specification provides a detailed description of the construction and use of a prognostic index of instant claim 1 (e) on pg 4, lines 20-28 and pg 5, lines 1-9, as follows:

> The invention also provides methods wherein the results of the determination of the levels of nuclear localization of p53, thrombospondin 1 expression, and the extent of microvascularization are used to prepare a prognostic or "risk" index for making a prognostic determination. In this aspect of the invention, a prognostic index is prepared comprising the product of the percentage of cells in the tumor sample that

> are positive for nuclear localization of p53 protein and one plus the intensity of immunohistochemical staining; the product of the percentage of cells in the tumor sample that are positive for microvascularization and one plus the intensity of immunohistochemical staining; and the product of the percentage of cells in the tumor sample that are positive for thrombospondin 1 expression and one plus the intensity of immunohistochemical staining. In calculating these products, the intensity of staining is assigned a value of 0 for staining equal to a negative control, a value of 1 for weak staining greater than the negative control, a value of 2 for moderate staining intensity, a value of 3 for staining intensity equal to a positive control, and a value of 4 for staining intensity greater than the positive control. The calculated products of each of the tumor marker determinations are then weighted on a scale of from +1 to -4, and the index is produced as the sum of the weighted products for nuclear localization of p53, thrombospondin 1 expression and microvascularization. In the practice of the invention, a prognosis of a likelihood of further neoplastic, particularly metastatic, disease is made when this sum is less than about -5.

Consequently, Applicants respectfully submit that the specification provides working examples and sufficient teaching and guidance to enable one of skill in the art to make and use the full scope of the claims.

Quantity of experimentation to make or use the invention based on the content of the disclosure:

The Action also states that "one of ordinary skill in the art would conclude that a method of making a prognosis by providing a prognostic index as recited in claim 1, step (e)...would require undue experimentation in order to use the invention as claimed." As pointed out above, Applicants respectfully submit that the specification provides detailed guidance and working examples for making and using a prognostic index as claimed. Thus, one of ordinary skill in the art would not need to engage in undue experimentation to carry out all the steps of the claimed invention.

For all of the reasons discussed above, Applicants submit that the claims satisfy the enablement requirement of 35 USC §112, first paragraph, and respectfully request reconsideration and withdrawal of the rejections.

CONCLUSION

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended or as originally presented. Allowance of the claims is thereby respectfully solicited.

If there are any questions or comments regarding this Response or application, the Examiner is encouraged to contact the undersigned representative as indicated below at 312-913-0001.

Applicants believe that no fees are due for this Response. If Applicants are mistaken, please charge any requisite fees to our Deposit Account, No. 13-2490.

Respectfully submitted,

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